ATTORNEY DOCKET NO. 2003080-0089 (SK-744-CON5)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Danishefsky, *et al.*	Examiner:	T. Solola
Serial No.:	10/058,695	Art Unit:	1626
Filed:	January 28, 2002		
For:	Synthesis of Epothilones, Intermediates Thereto, Analogues and Uses Thereof		

Box RCE
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

TRANSMITTAL

Enclosed please find the following documents regarding the above-referenced matter:

1) Transmittal Letter (1 pg.);
2) Request for Continued Examination (RCE) Transmittal w/copy
3) Amendment and Response
4) Interview Summary
5) Statement Filed Pursuant to the Duty of Disclosure Under 37 CFR §§1.56, 1.97 and 1.98
6) PTO-1449 (2 pages);
7) Check in the amount of $375.00 (RCE, Small Entity);
8) Return Postcard.

Please charge any fees or credit any overpayments to our Deposit Account No. 03-1721.

Respectfully submitted,

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ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, DC 20231

Sir:

INTERVIEW SUMMARY

Applicant thanks the Examiner for granting an in-person interview on November 19, 2002, for both USSN 09/874,514 and USSN 10/058,695. Both of these cases claim pharmaceutical compositions comprising an effective amount of an epothilone compound, and recite a particular concentration range that constitutes the "effective amount". In each case, the only remaining art rejection is a rejection for obviousness over Bollag *et al.* (*Cancer Research* 55:2325-2333, June 1, 1995).

Applicant and Examiner did not disagree about the content of Bollag *et al.*, which describes the tubulin-prolymerizing properties of Epo A and Epo B and *in vitro* testing of particular epothilone compounds, EpoA and EpoB, against cultured cells. The tested compound killed the cultured cells.

Applicant asserted that Bollag *et al.* provided at most an invitation to experiment, to determine whether one or more epothilone compounds could be identified that might be useful in a pharmaceutical context. However, Bollag *et al.* provide no reasonable expectation that such a compound could be identified. Bollag *et al.* show that EpoA and Epo B kills cultured cells. However, Bollag *et al.* does not show that Epo A and Epo B can kill tumor cells while sparing normal cells. Furthermore, Bollag *et al.* does not show that EpoA and EpoB can kill any kind of cells *in vivo*. Epothilones kill cells by binding to microtubules. A variety of compounds are known that bind to microtubules, many of which can kill cells. Very few such compounds can discriminate between normal and tumor cells. The teachings of Bollag *et al.* cannot and would not give a person of ordinary skill in the art *any* expectation that a therapeutically effective

amount of an epothilone *could possibly* exist. The present inventors not only demonstrated that such an amount *does* exist, they identified particular useful ranges and claimed pharmaceutical compositions containing those ranges. Applicant pointed out that, even if Bollag *et al. could* render obvious some pharmaceutical compositions (which it cannot), it certainly could not teach or suggest those pharmaceutical compositions containing the particular ranges of epothilones recited in Applicant's claims. Applicant further pointed out that Applicant's own inventors, who represent researchers of at least ordinary skill in the art and were aware of and relying on the information provided by Bollag *et al.*, had significant difficulty identifying a useful range of epothilones. In initial experiments, the inventors killed all of the mice tested. Bollag *et al.* did not provide any teaching or suggestion that it would be possible to avoid the same outcome with humans.

Examiner asserted that Applicant's claims were not patentable because they were directed to compositions and the only element of a composition that can ever impart patentability to a composition is the identity of the active ingredient. Applicant challenged this assertion and Examiner argued that some epothilones are natural products and it would be irresponsible for him to grant claims to Applicant to pharmaceutical compositions containing an epothilone when Applicant was not the first to identify an epothilone. Examiner pointed out that, if Patent Office practice were to allow such claims, then second-comers could obtain claims to pharmaceutical compositions that they could not make because someone else would own the underlying rights to the active ingredient. Applicant pointed out that freedom to operate considerations such as this are not relevant to patentability, but rather reflect business considerations for patent applicants.

Examiner agreed to discuss Applicant's arguments with his supervisor and with his quality control division, and indicated that he would contact Applicant in about a week.

Respectfully submitted,

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